Remarks

Priority:

The claims of priority to U.S. Patent 6,379,966 has been denied for lack of literal support for the term siRNA in the priority document. Applicants have amended the claims to obviate the rejection. Specifically, Applicants have amended the term siRNA to cite double strand oligonucleotide. Support for delivery of an oligonucleotide via intravascular injection is provided in the priority document at column 3 lines 23-26. Support for RNA is provided in the priority document at column 6 lines 18-20. That the RNA may be double stranded RNA is provided in the priority document at column 6 lines 35-36. That a polynucleotide may be delivered to cause inhibition of gene expression is provided in the specification at column 6 lines 40-43.

Rejection of the Claims under 35 USC § 112

It was noted by the Examiner that claims 13, 14, 17 and 18 depended from canceled claim 12. Applicants have amended claim 13 to make it depended on claim 11 to obviate the rejection.

Rejection of the claims under 35 USC § 103

Claims 11-18 have been rejected under 35 U.S. C. 103 as being unpatentable over Zimmer (Methods, 1999) in view of Elbashir et al (Nature 2001) and Zhang et al (Human Gene Therapy 1999). The Action notes that the instant claims do not recite any functional activity of the oligonucleotide following delivery to the cell. Applicants have amended claim 1 to recite that the RNA oligonucleotide inhibits expression of the gene in the cell, thus providing for a limitation of functional delivery of the oligonucleotide.

The action states that any injection into the tail vein is equivalent to increasing vessel permeability in the target tissue because the injection itself would inherently increase pressure in the area of injection at the time of injection and the tail vein can be considered to be the target tissue. Applicants respectfully disagree. Zimmer teaches that oligonucleotides injected into the tail vein accumulate (albeit non-functionally) in the liver. Thus, according to Zimmer, the liver would be the target tissue. However, the tail vein is not in the liver. Therefore, Zimmer does not teach increased permeability of vessels in the target tissue. Applicants teach that the

oligonucleotide is injected into an afferent or efferent vessel of the target tissue (page 3 lines 12-31). The Applicants further teach that hepatocytes (parenchymal cells of the liver, page 20 line 14) are targeted by injecting the polynucleotide into the tail vein of a rodent (page 4 lines 18-20). Thus, Applicants clearly teach that the tail vein itself and the tissue immediately around the injection point when injecting into the tail vein are not the target tissue. Applicants also teach delivery of double strand RNA to the quadricep (thigh) and gastrocnemius (calf) muscles following injection into the external iliac artery. The iliac artery is an afferent vessel of muscles in the hind limb. It is not possible for permeability at the injection point in the iliac artery, as caused by the needle, to result in delivery to the gastrocnemius muscle.

The Examiner's objections and rejections are now believed to be overcome by this response to the Office Action. In view of Applicants' amendment and arguments, it is submitted that claims 11 and 13-18 should be allowable.

Respectfully submitted,

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I hereby certify that this correspondence is being facsimile transmitted to the USPTO or deposited with the United States Postal Service with sufficient postage as express mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on this date: May 15, 2006

Kirk Ekena